Influenza: Overview for Healthcare Providers

Based on Recommendations of Advisory Committee for Immunization Practices (ACIP)

Organism	• Influenza virus – types A, B (A is further categorized into subtypes); type C - rare cause of disease
	• Frequent mutations of surface glycoprotein genes result in new influenza virus variants
	  o Antigenic shift → emergence of completely new subtypes (type A only; leads to pandemics)
	  o Antigenic drift → minor changes (all types; leads to frequent outbreaks & epidemics)

Reservoir	Type A – humans; swine; birds; types B & C – humans
Communicability	• Person-to-person, primarily through coughing and sneezing of infected persons • Communicable 1 day before onset of symptoms until approx. 5 days thereafter • Disease peaks in U.S. from December to March. • In pandemics, entire population susceptible; attack rates high among all ages
Mortality Rates	Deaths result from pneumonia and exacerbations of cardiopulmonary and other chronic conditions. • **Interpandemic years**: 1972 through 1992 - 9.1 deaths per 100,000 Americans per season • **Pandemics**: 1918 Spanish flu – 218.4 deaths per 100,000 Americans; 1957 Asian flu – 22 deaths per 100,000; 1968 Hong Kong flu – 13.9 deaths per 100,000
Incubation period	1-3 days
Symptoms	• Influenza A – Abrupt onset of fever, myalgia, headache, severe malaise, sore throat, rhinitis, nonproductive cough (symptoms last limited number of days; cough can persist for 2 weeks) • Influenza B – Similar but milder symptoms than type A; occurs primarily in children
Complications	High risk: Age 6-23 months., ≥65 yrs.; nursing home residents; persons w/ chronic cardiac, pulmonary, metabolic & renal conditions & hemoglobinopathies; immunocompromised; >12 wks of pregnancy • Pneumonia - secondary bacterial (most frequent) and primary influenza viral • Worsening of underlying medical conditions • Rarely associated with Reye syndrome (occurs primarily in children with Influenza B taking aspirin); myocarditis; encephalopathy; transverse myelitis; myositis; pericarditis
Laboratory tests	Rapid antigen tests; viral culture; serology; PCR; immunofluorescence
Infection control	Standard precautions, strict hand washing. For hospitalized cases: isolation; droplet precautions
Prevention	**Primary strategy**: Vaccination annually before influenza season • Antigenic drift necessitates annual reformulation of flu vaccine to incorporate new strains • Inactivated (i.e., killed) trivalent vaccine; approved for ages ≥6 months old • Live, attenuated trivalent vaccine; approved for healthy individuals 5-49 years who are not pregnant • Provides protection in 70-90% healthy adults <65 years old; reduces complications by 50-60% and death by 80% among elderly in nursing homes • Contraindications – allergy to egg or vaccine; avoid in persons with previous severe reaction • Delay vaccination of persons with acute febrile illness but not minor illness, with or without fever **Adjunct strategy**: Chemoprophylaxis with antivirals for unvaccinated high risk & advanced HIV

Note. Information in Appendix H was taken from: Centers for Disease Control and Prevention. Prevention and Control of Influenza: Recommendations of the Advisor Committee on Immunization Practices. MMWR: July 28, 2006 / 55;1-41].

<table>
<tr><td>Vaccine Recommendations</td><td colspan="5">• September: High risk groups and first vaccine for ages 6 months to 9 years (because requires series of 2 vaccines); October-November: all patients (high risk and healthy), healthcare workers; December and later: continue to offer (adults develop protection two weeks after vaccination)</td></tr>
<tr><td rowspan="5">Antiviral Recommendations</td><td>Antiviral Agent</td><td>Trade Name</td><td>Flu type</td><td>Use</td><td>Age Restrictions</td></tr>
<tr><td>Zanamivir</td><td>Relenza®</td><td>A and B</td><td>Prophylaxis
Treatment</td><td>≥5 years
≥7 years</td></tr>
<tr><td>Oseltamivir</td><td>Tamiflu®</td><td>A and B</td><td>Prophylaxis/Treatment</td><td>≥1 year</td></tr>
<tr><td colspan="5">Treatment: Can reduce duration of uncomplicated illness if given within 48 hours of symptom onset.</td></tr>
<tr><td colspan="5"></td></tr>
<tr><td>Surveillance</td><td colspan="5">State regulations require the reporting of influenza cases to the health department within 3 days.</td></tr>
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Influenza Antivirals: Overview for Healthcare Providers

Amantadine Manufactured under the trade name Symmetrel® by Endo Laboratories Also available in generic forms	• Used to treat uncomplicated illnesses due to influenza A in individuals 1 year of age and older (must be given within two days of illness onset) • Used prophylactically to reduce chance of getting influenza A in individuals 1 year of age and older (approximately 70%-90% effective) • Also used in the treatment of Parkinson's disease and drug-induced extrapyramidal reactions • Available in tablet or syrup form • Reported adverse reactions include nervousness, anxiety, nausea, dizziness, and insomnia • More serious but less frequent side effects including behavioral changes, delirium, hallucinations, agitation, and seizures have been observed among individuals with renal insufficiency, seizure disorders, or certain psychiatric disorders • Should not be used for patients with untreated angle closure glaucoma because of anticholinergic effects. Observe patients with seizure disorders closely for possible increased seizure activity • To reduce the emergence of antiviral drug-resistant viruses, amantadine therapy for treatment of influenza should be discontinued as soon as clinically warranted, typically after 3-5 days of treatment or within 24-48 hours after disappearance of signs and symptoms • **Because a large number of influenza isolates tested at CDC have developed resistance, CDC has recommended against use of amantadine for the treatment or prophylaxis of influenza.**
Rimantadine Manufactured under the trade name Flumadine® by Forest Pharmaceuticals, Inc.	• Used to treat uncomplicated illnesses due to influenza A in adults (must be given within two days of illness onset) • Used prophylactically to reduce chance of getting influenza in individuals 1 year of age and older (approximately 70%-90% effective) • Available in tablet or syrup form • Adverse events reported most frequently include insomnia, dizziness, headache, nervousness, fatigue, nausea, vomiting, anorexia, dry mouth, abdominal pain, and asthenia • To reduce the emergence of antiviral drug-resistant viruses, rimantadine therapy for treatment of influenza should be discontinued as soon as clinically warranted, typically after 3-5 days of treatment or within 24-48 hours after disappearance of signs and symptoms • **Because a large number of influenza isolates tested at CDC have developed resistance, CDC has recommended against use of rimantadine for the treatment or prophylaxis of influenza.**
Zanamivir Manufactured under the trade name Relenza® by Glaxo Wellcome, Inc.	• Used for prophylaxis to reduce the risk of influenza A or B in individuals 5 years of age and older. • Used to treat uncomplicated illnesses due to influenza A and B in individuals 7 years of age and older (must be given within two days of illness onset) • Available as a dry powder, inhaled from a breath-activated plastic device called a Diskhaler • Side effects may include headache, diarrhea, nausea, vomiting, nasal irritation, bronchitis, cough, sinus inflammation, infections of the ear, nose, and throat, and dizziness. • Some patients, especially those with asthma or chronic obstructive pulmonary disease (COPD), have had bronchospasm or serious breathing problems after using zanamivir • Since Zanamivir has not been shown to shorten the duration of influenza in people with these diseases, and because of the risk of serious adverse effects, zanamivir is not generally recommended for people with chronic respiratory diseases such as asthma or COPD • Patients with underlying respiratory disease should have a fast-acting inhaled bronchodilator available when taking zanamivir • Recommended duration of treatment is 5 days
Oseltamivir Manufactured under the trade name Tamiflu® by Roche Laboratories, Inc.	• Used for prophylaxis to reduce the risk of influenza A or B in individuals 1 year of age and older • Used to treat uncomplicated illnesses due to influenza A and B (must have been given within two days of illness onset) in individuals 1 year of age and older • Available in capsule or oral suspension form • Possible side effects include: nausea, vomiting, diarrhea, bronchitis, stomach pain, dizziness, and headache. Side effects are similar whether taken for treatment or prophylaxis • Recommended duration of treatment is 5 days

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Recommendations for Use of Antivirals

Chemoprophylaxis is not a substitute for vaccination. However, in the event of an influenza pandemic, vaccine may not be available, or may only be available in limited quantities.

In the United States, four antiviral agents are approved for preventing and treating influenza: amantadine, rimantadine, zanamivir, and oseltamivir. **Note: because a significant proportion of recent influenza isolates tested at CDC have developed resistance to the M2 inhibitors (amantadine and rimantadine), the CDC has recommended against the use of either amantadine or rimantadine for the treatment or prophylaxis of influenza.**

Some important points about influenza antiviral medications are:

- Benefits of using antiviral agents in the treatment of influenza are limited.
- When administered within two days of illness onset, antivirals may reduce duration of uncomplicated influenza illness by approximately one day.
- None of the four antiviral agents have been demonstrated to be effective in preventing serious influenza-related complications such as bacterial or viral pneumonia.
- Death from influenza is much more likely to occur in the event of a serious influenza-related complication, especially among high-risk individuals. Preventing influenza rather than attempting to shorten the duration of illness can achieve maximum benefit. Therefore, in the event of an influenza pandemic, use of antivirals should be prioritized for prophylactic rather than treatment purposes.

Recommendations for chemoprophylaxis are provided primarily to help health care-providers make decisions regarding persons who are at greatest risk of severe illness and complications from influenza. Prophylactic use of antivirals may be considered for the following groups:

1. Persons at high risk who should not be vaccinated, including those with anaphylactic hypersensitivity to eggs or other components of the influenza vaccine, or individuals not at high risk for severe influenza complications and who are known to have experienced GBS within 6 weeks after a previous influenza vaccination
2. Unvaccinated persons aged ≥ 65 years of age
3. Unvaccinated residents of nursing homes and other chronic-care facilities that house individuals of any age with chronic medical conditions
4. Unvaccinated adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including children with asthma
5. Unvaccinated adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression caused by medications or by human immunodeficiency virus

6. Unvaccinated children and adolescents (aged 1 -18 years) who are receiving long-term aspirin therapy and therefore may be at risk of developing Reye syndrome after influenza infection
7. Unvaccinated employees of nursing homes, chronic-care facilities, and assisted living residences who have contact with patients or residents
8. Unvaccinated individuals who provide home care to persons at high-risk
9. Unvaccinated household members (including children ≥1 year of age) of persons at high-risk
10. Persons aged ≥50 years and others at high risk traveling to the tropics, in organized tours, or to the southern hemisphere during the summer
11. Persons at high risk who are vaccinated after influenza activity has begun in the community until immunity has developed (duration: two weeks)
12. Children aged <9 years who receive influenza vaccine for the first time (duration: until two weeks after second dose of influenza vaccine)
13. Persons who provide care to those at high risk during an outbreak caused by a variant strain of influenza that might not be controlled by the vaccine, regardless of vaccination status
14. All residents of an institution or other semi-enclosed settings that houses many high-risk individuals during an outbreak, regardless of whether they received influenza vaccinations during the previous fall

Pregnant Women

Although women who will be pregnant during the influenza season should be vaccinated, this group is not recommended for routine antiviral treatment. No clinical studies have been conducted regarding the safety and efficacy of amantadine, rimantadine, zanamivir, or oseltamivir for pregnant women. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these four drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

Drug Resistance

To limit the potential transmission of drug-resistant virus during institutional outbreaks, measures should be taken to reduce contact as much as possible between persons taking antiviral drugs for treatment and other persons, including those taking the same drugs for chemoprophylaxis.

Combination of Antiviral Medications

No published data are available concerning the safety or efficacy of using combinations of any of these four influenza antiviral drugs. For more detailed information concerning potential drug interactions for any of these influenza antiviral drugs, the package insert should be consulted.

It is important to be aware of persons already taking one of these medications for another purpose (e.g., amantadine for Parkinson's disease) so that they will not be prescribed an additional amount, and thus receive too large a dose of the drug.